Clinical Policy Title:	pemigatinib
Policy Number:	RxA.635
Drug(s) Applied:	Pemazyre®
Original Policy Date:	07/05/2020
Last Review Date:	07/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Pemigatinib (Pemazyre®) is a kinase inhibitor indicated for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pemigatinib (Pemazyre®)	Unresectable locally advanced or metastatic cholangiocarcinoma	13.5 mg orally once daily for 14 consecutive days followed by 7 days off therapy in 21-day cycles. Continue treatment until disease progression or unacceptable toxicity occurs Severe renal impairment and Hepatic Impairment: 9 mg orally once daily for 14 consecutive days followed by 7 days off therapy in 21-day cycles.	13.5 mg/day

Dosage Forms

- Oral Tablets: 4.5 mg, 9 mg, and 13.5 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Unresectable locally advanced or metastatic cholangiocarcinoma (must meet all):

1. Diagnosis of unresectable locally advanced or metastatic cholangiocarcinoma;
2. Positive result of FDA-approved test to determine fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Patient must have tried and failed at least 1 regimen as recommended by NCCN.
6. Request meets one of the following (a or b):
   a. Dose does not exceed 13.5 mg/day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (Prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Myeloid/Lymphoid Neoplasms with Eosinophilia & Tyrosine Kinase Fusion Gene (off-label) (must meet all):
1. Diagnosis of Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Gene;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Positive result of FDA-approved test to determine fibroblast growth factor receptor 1 (FGFR1) in chronic phase or blast phase;
5. Request meets one of the following (a or b):
   a. Treatment with a preferred clinical trial rather than off-label use;
   b. Treatment in combination with ALL- or AML-type induction chemotherapy followed by allogeneic HCT (if eligible) for lymphoid, myeloid or mixed lineage neoplasms with eosinophilia and FGFR1 rearrangement in blast phase;
7. Request meets one of the following (a or b):
   a. Dose does not exceed 13.5 mg/day.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (Prescriber must submit supporting evidence).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Pemazyre® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 13.5 mg/day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use. (Prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FGFR2: Fibroblast growth factor receptor 2
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
ALL: Acute lymphoblastic leukemia
AML: Acute myeloid leukemia
HCT: Hematopoietic cell transplantation
OCT: Optical coherence tomography
PFS: Progression free survival
MDRD: Modification of Diet in Renal Disease
AST: Aspartate aminotransferase

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
5-fluorouracil + oxaliplatin	Varies	Varies
cisplatin and gemcitabine	25 mg/m^2 intravenous on days 1 and 8 in combination with gemcitabine (1,000 mg/m^2 intravenous on days 1 and 8) every 21 days for 8 cycles.	cisplatin: 100 mg/m^2 gemcitabine: 1,250 mg/m^2 intravenous once weekly;
5-fluorouracil + cisplatin	Varies	Varies
capecitabine (Xeloda®) + cisplatin	Varies	Varies
capecitabine (Xeloda®) + cisplatin	Varies	Varies
capecitabine (Xeloda®) + oxaliplatin	Varies	Varies
gemcitabine + Abraxane®	Varies	Varies
gemcitabine + capecitabine (Xeloda®)	Varies	Varies
gemcitabine + oxaliplatin	Varies	Varies
5-fluorouracil	Varies	Varies
capecitabine (Xeloda®)	Varies	Varies
FOLFOX (5-fluorouracil, leucovorin, oxaliplatin)	Varies	Varies

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - None Reported.

- Boxed Warning(s):
  - None Reported.

APPENDIX D: General Information

- Ocular Toxicity: Pemazyre® can cause retinal pigment epithelial detachment. Perform ophthalmological examination including optical coherence tomography (OCT) prior to initiation of therapy, every 2 months for the first 6 months of treatment and every 3 months thereafter, and urgently at any time for visual symptoms.
- Hyperphosphatemia and Soft Tissue Mineralization: Pemazyre® can cause hyperphosphatemia leading to soft tissue mineralization, cutaneous calcification, calcinosis, and non-uremic calciphylaxis. Monitor for hyperphosphatemia and withhold, reduce the dose, or permanently discontinue based on duration and severity of hyperphosphatemia.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of reproductive potential of the potential risk to the fetus and use effective contraception.
- Renal impairment (severe, estimated GFR 15 to 29 mL/min/1.73 m(2), estimated by Modification of Diet in Renal Disease (MDRD))
- Hepatic impairment (severe, total bilirubin greater than 3x ULN with any AST)

References

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2. Pemigatinib. Lexi-Drugs. Hudson, OH: Lexicomp, 2020. https://online.lexi.com/lco/action/search?q=pemigatinib&t=name&va=pemigatinib . Updated March 27, 2022. Accessed April 07, 2022.
3. National Comprehensive Cancer Network Guidelines. Hepatobiliary Cancers Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed April 07, 2022.
4. National Comprehensive Cancer Network Guidelines. Myeloid/Lymphoid Neoplasms with Eosinophilia & Tyrosine Kinase Fusion Gene Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mlne.pdf . Published August 21,2020. Accessed April 07, 2022.
5. Abou-Alfa GK, Sahai V, Hollebecque A, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study [published online March 20, 2020]. *Lancet Oncol*. doi:10.1016/S1470-2045(20)30109-1. Available at: https://pubmed.ncbi.nlm.nih.gov/32203698/. Accessed April 07, 2022.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	07/05/2020	09/14/2020
Policy was reviewed: 1. Clinical Policy Title was updated to include Last Review Date. 2. Dosing Information was updated to include indication “Unresectable locally advanced or metastatic cholangiocarcinoma”. 3. Dosing Information dosing regimen was updated to include renal and hepatic impairment dosing “Severe renal impairment and Hepatic Impairment: 9 mg orally once daily…”.	07/02/2021	09/14/2021

4. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 5. Initial Approval Criteria I.A.6 was updated to include “Maximum dose does not exceed 13.5 mg/day”. 6. Initial Approval Criteria I.B was updated to include off-label indication “Myeloid/Lymphoid Neoplasms with Eosinophilia & Tyrosine Kinase Fusion Gene (off-label)”. 7. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 8. Continued Therapy Approval Criteria II.A.3 was updated to include “Maximum dose does not exceed (a or b)…”. 9. Continued Therapy Approval Criteria II.A.3.a was updated to include “Cholangiocarcinoma: 13.5 mg/day”. 10. Continued Therapy Approval Criteria II.A.3.b was updated to include “Myeloid/Lymphoid Neoplasms: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence)”. 11. Appendix A was updated to include abbreviations NCCN, ALL, AML, HCT, OCT, and PFS. 12. Appendix B: Therapeutic Alternatives was updated from “There are no FDA approved medications for previously treated…” to “Not Applicable”. 13. Appendix D: General Information was updated to include “Ocular Toxicity: Pemazyre® can cause retinal pigment epithelial detachment…”, “Hyperphosphatemia and Soft Tissue Mineralization: Pemazyre® can cause hyperphosphatemia…”, “Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients…”, “Renal impairment (severe, estimated GFR 15 to 29 mL/min/1.73 m(2), estimated…”, and “Hepatic impairment (severe, total bilirubin greater than 3x ULN with any AST)”. 14. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.6. and I.B.7: Updated dosing criteria from Maximum dose does not exceed 13.5 mg/day to Request meets one of the following (a or b):	04/07/2022	07/18/2022

a. Dose does not exceed 13.5 mg/day. b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (Prescriber must submit supporting evidence). 2. Continued Therapy Approval Crtieria, II.A.3: Updated dosing criteria from Maximum dose does not exceed (a or b): a. Cholangiocarcinoma: 13.5 mg/day; b. Myeloid/Lymphoid Neoplasms: Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). to If request is for a dose increase, request meets one of the following (a or b): a. New dose does not exceed 13.5 mg/day; b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use. (prescriber must submit supporting evidence). 3. Appendix A: Updated to include abbreviations MDRD & AST. 4. Appendix B, Drug Name: Updated to include new therapeutic alternative. 5. References were reviewed and updated.		